

Atty. Docket 1385.45510VX1  
Application Serial No. 10/087,942  
Office Action dated April 28, 2005

### Remarks

#### **I. Introduction**

By the present Amendment, claim 128 has been amended. No claims have been added or cancelled. Accordingly, claims 2-15, 18-30, and 128 remain pending in the application. Claim 128 is independent.

#### **II. Interview Summary**

Applicants and their representatives thank the Examiner for the courtesy and cooperation extended during the interview conducted on June 20, 2005 at the U.S. Patent and Trademark Office. Present at the interview were Examiner Eric S. DeJong, Ph.D., Primary Examiner John S. Brusca, Ph.D., Leonid D. Thenor, and Belinda Lew, Ph.D.

During the interview, Applicants provided a PowerPoint presentation as an overview of the invention and methodology. Claims 2-15, 18-30, and 128 were discussed with respect to all rejections of record. The claims were also discussed in general and with respect to Lam et al. Examiner Brusca discussed the manner in which a whole molecule parameter could be interpreted as a sequence-specific parameter if additional amino acids were added or removed from a particular peptide. The term "relationship" was indicated as being broad relative to the disclosure. It was also indicated that the claims did not specify that the second test library could contain members that were not present in the first test library. It was indicated that Lam identified peptides of different lengths as well as a second library that contained members from the first library. It was also indicated that the specification did not provide adequate support for using compounds such as steroids and nucleic acids.

Various possible amendments were discussed that could potentially address issues raised under 35 U.S.C. §112, second paragraph and 35 U.S.C. §102(b). No agreements were reached on claim amendments.

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### **III. Office Action Summary**

In the Office Action of April 28, 2005, claim 30 was rejected under 35 U.S.C. §112, first paragraph as failing to comply with the enablement requirement. Claims 128, 3-10, 13-15, and 18-28 were rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent 5,510,240 issued to Lam et al. ("Lam"). Claims 128 and 2 were rejected under 35 U.S.C. §103(a) as being unpatentable over Bause. Claims 128, 11, and 12 were rejected under 35 U.S.C. §103(a) as being unpatentable over Lam in view of Vyas et al. ("Vyas"). Claims 128, 19, 23, 28, and 29 were rejected under 35 U.S.C. §103(a) as being unpatentable over Lam in view of Davis et al. ("Davis"). These rejections are respectfully traversed.

### **IV. Rejections under 35 U.S.C. §112, first paragraph**

Claim 30 was rejected under 35 U.S.C. §112, first paragraph as failing to comply with the enablement requirement. Regarding this rejection, the Office Action indicates that the specification did not provide specific guidance for practicing the invention.

Applicants, respectfully disagree. The present invention is directed to a system and method for reducing the amount of actual experimentation required to identify specific compounds having desired properties. As discussed in the specification, these compounds can include peptides, proteins, carbohydrates, nucleic acids, and lipids (e.g., free fatty acids, triglycerols, steroids). See paragraphs [0022], [0063], and [0150] of the published application. The application aptly describes the steps required to accomplish this reduction in experimentation.

Applicants therefore respectfully submit that claim 30 satisfies the requirements of 35 U.S.C. §112, first paragraph. Withdrawal of this rejection is respectfully requested.

### **V. Rejections under 35 U.S.C. §102**

Claims 128, 3-10, 13-15, and 18-28 were rejected under 35 U.S.C. §102(b) as being anticipated by Lam. In support of this rejection, the Office Action indicates that Lam discloses all the steps recited in the claimed invention. The Office Action also provides citations to various passages in Lam that supposedly teach the claimed steps. Applicants respectfully disagree.

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As amended, independent claim 128 defines a method of identifying a culture medium component that comprises the steps:

- identifying a predetermined set of test compounds;
- parameterizing the predetermined set of test compounds by determining at least one parameter for each test compound in the predetermined set of test compounds;
- performing a space-filling design of the parameterized predetermined set of test compounds to identify a plurality of first test compounds, wherein the plurality of first test compounds is a subset of the predetermined set of test compounds;
- constructing a first test library comprising a plurality of first culture media, each of which contains a respective first test compound;
- determining a property, having an indicia, of the plurality of first culture media;
- measuring the indicia of the property of the plurality of first culture media;
- determining a quantitative relationship between the measured indicia of the property, and at least one parameter of the plurality of first test compounds;
- calculating an estimated indicia for a plurality of candidate culture media using the determined quantitative relationship, wherein each candidate culture medium contains a respective candidate test compound from the predetermined set of test compounds that is not in the first test library;
- setting a test requirement having a test indicia range;
- selecting a second test library comprising at least one second culture medium, wherein each second culture medium is a candidate culture medium having an estimated indicia that satisfies the test requirement;
- measuring the indicia of the property of the at least one second culture medium; and
- identifying at least one second culture medium having a measured indicia that satisfies the test requirement.

According to the invention defined by independent claim 128, a predetermined set of test compounds is identified. A subset (i.e., smaller number) of the predetermined test compounds is then selected to be parameterized through determination of at least one parameter. The parameter can correspond to various properties of the test compounds. A space-filling design is then performed for the parameterized subset of test compounds. A first test library is constructed to include a plurality of first culture media. Each of the first culture medium contains at least one first test compound identified using the space-filling design. Furthermore, the plurality of first test compounds is a subset of the predetermined set of test compounds. Next, a quantitative relationship is derived between a measured indicia of

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the first culture media and at least one parameter of the first test compounds. The indicia can reflect, under certain circumstances, a value for a desired property of the first culture media. According to one or more embodiments of the invention, the relationship can have a mathematical component capable of being applied to other (untested) culture media.

Next, an estimated indicia is calculated for a plurality of candidate culture media using the derived relationship. The candidate culture media each contain a respective candidate test compound from the predetermined set of test compounds. Furthermore, the candidate test compounds are not used in the first test library. A test requirement is set with an indicia range. The test requirement can be set based on desired properties, characteristics, or specific research being performed. A second test library is selected to include at least one second culture medium. Each of the second culture medium corresponds to a candidate peptide having an estimated indicia that satisfies the test requirement. Next, the indicia of each second culture medium is actually measured. Second culture media having a measured indicia that satisfies the test requirement are subsequently identified.

As can be appreciated, one or more embodiments of the invention provide a candidate library that contains actual lead compounds expected to have certain desired properties. This expectation is based on the indicia calculated (or estimated) using the derived relationship. The culture media containing these lead compounds can subsequently be tested to confirm the presence of these desired properties. This can be particularly useful, for example, in situations where a high number of test compounds exist (e.g., peptide identification). It can often be expensive and time consuming to test culture media containing individual test compounds to identify those having desired properties using conventional methods. Thus, the actual number of experiments conducted can be significantly reduced through application of the invention defined by independent claim 128.

The claimed invention can be used, in part, to reduce time and costs by predicting a subset of test compounds (from a very large library of test compounds) that will have the desired properties. Users are able to consider the use of culture media, containing a substantially large group of test compounds, that could potentially have an indicia which satisfies the test requirement. The first test library can then be filtered to a smaller candidate library. A user would then take the compounds identified in the candidate library and

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conduct actual experimentation to obtain more accurate values for the desired properties of the culture media.

Contrary to the assertions made in the Office Action, Lam fails to reveal any disclosure or suggestion for various features recited in independent claim 128. Lam discloses a method of screening a peptide library. Lam provides assays for biological activity of a bio-oligomer from a library treated for removing any toxic molecules remaining from synthesis. The biological activities assayed can include toxicity and killing, stimulation and growth promotion, and physiological change.

Lam does not construct a first test library as set forth in the claimed invention. Lam does not parameterize predetermined test compounds by determining a specific parameter for each test compound, and then perform a space-filling design of the parameterized test compounds. Lam fails to provide a library of first culture media that contain at least one first test compound identified by the space-filling design. This is to be expected since no space-filling design methodology is applied. Furthermore, Lam does not mention or suggest deriving a quantitative relationship between a measured indicia and at least one parameter of the test compound (or peptide).

Lam further provides a second round of screening where a second library is synthesized. However, the second library is "based on the common sequences of the ligands selected during the first screening." See col. 17, lines 19-24, emphasis added. Lam appears to identify higher levels of activity by merely setting a more stringent threshold level for re-screening selected ligands identified in the first library. Lam further discusses suspension of beads in a well, and subsequent release of a peptide to exert a biological activity. Beads from wells with biological activities are then sequenced and tested to determine which particular sequence demonstrated biological activity. See col. 22, lines 20-31. Accordingly, Lam does not apply a quantitative relationship to estimate the indicia of candidate test compounds that are not in the first test library (i.e., ligands that were not screened during the first round, or beads that were not in the library).

It is therefore respectfully submitted that independent claim 128 is allowable over the art of record.

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Claims 3-10, 13-15, and 18-28 depend, either directly or indirectly, from independent claim 128, and are therefore believed allowable for at least the reasons set forth above with respect to independent claim 128. In addition, these claims each introduce novel elements that independently render them patentable over the art of record.

**VI. Rejection under 35 U.S.C. §103**

Claims 128 and 2 were rejected under 35 U.S.C. §103(a) as being unpatentable over Bause. Applicants presume this rejection to be based on a combination of Lam and Bause, because the Office Action goes on to describe features disclosed by Lam. The Office Action admits that Lam fails to disclose consideration of space-filling parameters. Bause is relied upon as disclosing this feature.

As previously discussed, Lam fails to disclose specific features of the claimed invention, including derivation of a quantitative relationship and application of such relationship to estimate the indicia of candidate culture media. While Bause discusses a space-filling model of a particular hexapeptide, such a model does not appear to correspond to a space-filling design that is intended to represent, for example, a peptide/compound space. Rather, it appears to be a three-dimensional structure of the peptide which identifies potential sugar-attachment sites. Notwithstanding this, there is simply no suggestion or motivation to combine the two references to arrive at the claimed steps. The combination of Lam and Bause simply fails to suggest features of the claimed invention, such as:

- determining a quantitative relationship between the measured indicia of the property, and at least one parameter of the plurality of first test compounds;

- calculating an estimated indicia for a plurality of candidate culture media using the determined quantitative relationship, wherein each candidate culture medium contains a respective candidate test compound from the predetermined set of test compounds that is not in the first test library;

- setting a test requirement having a test indicia range;

- selecting a second test library comprising at least one second culture medium, wherein each second culture medium is a candidate culture medium having an estimated indicia that satisfies the test requirement;

- measuring the indicia of the property of the at least one second culture medium; and

- identifying at least one second culture medium having a measured indicia that satisfies the test requirement.

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It is therefore respectfully submitted that independent claim 128 is allowable over the art of record.

Claim 2 depends from independent claim 128, and is therefore believed allowable for at least the reasons set forth above with respect to independent claim 128. In addition, claim 2 introduces novel elements that independently render it patentable over the art of record.

Claims 128, 11, and 12 were rejected under 35 U.S.C. §103(a) as being unpatentable over Lam in view of Vyas. Claims 128, 19, 23, 28, and 29 were rejected under 35 U.S.C. §103(a) as being unpatentable over Lam in view of Davis. The Office Action asserts that Vyas discloses the use of analytical techniques such as space-filling designs. Davis is relied upon as disclosing analysis of a peptide that is a toxin. However, the inclusion of secondary references, such as Vyas and Davis, does not remedy the failure, by Lam, to disclose features recited in independent claim 128. Specifically, the applied references fail to disclose or suggest various features, such as:

- determining a quantitative relationship between the measured indicia of the property, and at least one parameter of the plurality of first test compounds;

- calculating an estimated indicia for a plurality of candidate culture media using the determined quantitative relationship, wherein each candidate culture medium contains a respective candidate test compound from the predetermined set of test compounds that is not in the first test library;

- setting a test requirement having a test indicia range;

- selecting a second test library comprising at least one second culture medium, wherein each second culture medium is a candidate culture medium having an estimated indicia that satisfies the test requirement;

- measuring the indicia of the property of the at least one second culture medium; and

- identifying at least one second culture medium having a measured indicia that satisfies the test requirement.

It is therefore respectfully submitted that independent claim 128 is allowable over the art of record.

Claims 11, 12, 19, 23, 28, and 29 depend from independent claim 128, and are therefore believed allowable for at least the reasons set forth above with respect to independent claim 128. In addition, these claims each introduce novel elements that independently render them patentable over the art of record.

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**VII. Conclusion**

For the reasons stated above, it is respectfully submitted that all of the pending claims are now in condition for allowance. Therefore, a Notice of Allowance is believed in order, and courteously solicited.

If the Examiner believes that there are any matters which can be resolved by way of either a personal or telephone interview, the Examiner is invited to contact Applicants' undersigned attorney at the number indicated below.



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Authorization

If the Examiner believes that there are any matters which can be resolved by way of either a personal or telephone interview, the Examiner is invited to contact Applicants' undersigned attorney at the number indicated below.

Applicants request any shortage or excess in fees in connection with the filing of this paper, including extension of time fees, and for which no other form of payment is offered, be charged or credited to Deposit Account No. 01-2135 (Case: 1385.45510VX1).

Respectfully submitted,

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